REMARKS/ARGUMENTS

Status of the Claims

Claims 1-3, 11, 18, 36, 41, 43, 44, 54-62, 89 and 95-101 were previously pending and presented for examination. Claims 4-10, 12-17, 19-35, 42, 45-53, 63-88, and 90-94 were canceled previously without prejudice. Claims 1, 2, 18, 43, 44, 61, and 98-100 are amended herein. Claims 102-111 are newly presented.

After entry of these amendments claims 1-3, 11, 18, 36, 41, 43, 44, 54-62, 89 and 95-111 will be pending and presented for examination.

Claims 43-44, 54-60, 96-97, 99 and 101 stand rejected as allegedly not enabled pursuant to 35 U.S.C. §112, first paragraph.

Claim 36 stands rejected as allegedly indefinite pursuant to 35 U.S.C. §112, second paragraph.

Claims 61 and 62 stand rejected as allegedly anticipated by Ishii et al. CAPLUS Abstract 108:177077 (1998) pursuant to 35 U.S.C. §102(b).

Claims 61 and 62 stand rejected as allegedly anticipated by Nazareth et al. CAPLUS Abstract 102:109290 (1985) pursuant to 35 U.S.C. §102(b).

Claims 1, 2, 36, 43, 44, 58, 59, 61, 62, 89, and 97 stand rejected as allegedly anticipated by Iwata et al. CAPLUS Abstract 116:214490 (1992) pursuant to 35 U.S.C. §102(b).

Claims 61 and 62 stand rejected as allegedly anticipated by Posner et al. CAPLUS Abstract 107:23211 (1987) pursuant to 35 U.S.C. §102(b).

Claims 61 and 62 stand rejected as allegedly unpatentable over Saupe et al. (U.S. Patent No. 4,881,969 pursuant to 35 U.S.C. §103(a).

Claims 3, 11, 18, 41, 95, 98, and 100 stand objected to as depending from a rejected base claim but were held to be allowable if rewritten in independent claim format.

Applicants thank the Examiner for indicating the subject matter deemed to be allowable and respectfully respond to the other grounds for rejection below.

Support for the Amendments to the Claims

Base pharmaceutical composition claim 1 and base method of treatment claim 43 were amended to delete the recital of "wherein said compound has pharmaceutical activity." Support for the subject matter of the amended claims is found in the previous version of the claims.

Support for the subject matter of amended pharmaceutical composition claim 2 and amended methods claim 44 is found in the previous version of these claims.

Claims 18, 98, and 99 were amended to delete the recital of 2,3-Dihydro-5-pentafluorophenylsulfonamidoindole.

Claim 43 was further amended to delete the recital of "preventing." Support for this amendment is found *inter alia* in the previous version of the claim.

Claim 61 was amended to recite "wherein R^2 is an optionally substituted heteroaryl group having only one or only two heteroatoms in the heteroaryl ring system thereof." Support for this subject matter is found *inter alia* in the specification at p. 14, line 8 which sets forth from one to four such heteroatoms; in Examples 15, 16, and 36 which set forth examples of compounds having one or two such heteroatoms; and in the specification at p. 14, second full paragraph. The provisos of the base claims also refer to such subject matter.

Claim 61 was further amended to recite "substituted or unsubstituted (C2-C10) alkyl" as a member of the R^1 Markush group. Support for this subject matter is found *inter alia* in original claim 41 and also pending claim 100.

Claim 61 was further amended to delete various heteroaryl members of the R^1 Markush group. Support for this subject matter is found in the previous version of the claim.

Claim 61 was further amended to recite the proviso that heteroaryl is other than 4-pyrimidyl. Support for this recital is found *inter alia* in the specification at p.15, line 17 which positively recites 4-pyrimidyl. Applicants note the positive recital adequately supports such a proviso pursuant to MPEP §2173.05(i) at p. 2100-215:

> Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d

> 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) ("[the] specification, having described the whole, necessarily described the part remaining."). See also *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), *aff 'd mem.*, 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Note that a lack of literal basis in the specification for a negative limitation may not be sufficient to establish a *prima facie* case for lack of descriptive support. *Ex parte Parks*, 30 USPQ2d 1234, 1236 (Bd. Pat. App. & Inter. 1993)...

Claims 98 and 99 were amended to delete a duplicative recital of 5-pentafluorophenylsulfonamidoindazole.

Claim 100 was amended to change its dependency from claim 62 to 61. Support is found *inter alia* in the previous version of the claim.

New claims 102 and 103 depend from claim 1 and 43 respectively and recite "wherein said compound is capable of increasing LDL receptor gene expression in a cell." Support is found *inter alia* in Example 72 at p. 70.

New claim 104 depends from claim 43 and recites "R^2 is a monocyclic heteroaryl group." Support for such subject matter is found *inter alia* in the specification at p. 14, line 7.

New claim 105 depends from claim 43 and sets forth R^2 heteroaryl group subject matter having one heteroatom in the heteroaryl ring system. Support for this subject matter is found *inter alia* in the specification at p. 14, line 8.

New claim 106 depends from claim 61 and recites "A method of reducing the level of low density lipoprotein particles levels or cholesterol in the blood of a mammalian subject in need thereof, which method comprises administering to said subject a therapeutically effective amount of a composition containing a compound of Claim 61, wherein said method said level of low density lipoprotein particles or cholesterol is reduced." Support for the indication subject matter is found in the objects of the invention as set forth on pages 4 and 5 of the specification. Support for the compound subject matter is as set forth as above for claim 61.

New claim 107 depends from claim 106 and recites that the subject is human. Support for this subject matter is found *inter alia* in the specification at original claim 59.

New claim 108 depends from claim 61 and sets forth heteroaryl subject matter recited at p. 14, lines 14-19.

New claims 109 and 110 depend from claim 108 and set forth limitations of pending compound claims 62 and 89.

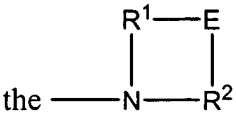
New claim 111 depends from claim 61 and recites the proviso that R^1 is other than unsubstituted C2-C10 alkyl. Support for this subject matter is found in the previous version of the claim. Applicants note the positive recital adequately supports such a proviso pursuant to MPEP §2173.05(i) at p. 2100-215.

In view of the above, the Applicants believe the amendments to the claims add no new matter and respectfully request their entry.

Response to the Rejection of Claims 43-44, 54-60, 96-97, 99 and 101 for Alleged Lack of Enablement of the "Preventing" Subject Matter

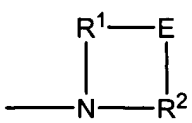
Without acquiescing to the position of the Examiner, and in order to facilitate prosecution of the instant application, Applicants have amended base claim 43 to delete the recital of "preventing." Applicants believe this amendment renders renders this grounds of rejection moot and respectfully request reconsideration.

Response to the Rejection of Claim 36 on Grounds of Alleged Indefiniteness.

The Examiner considered the  member as recited in Claim 36 to lack antecedent basis in Claim 2.

Applicants note that antecedent basis can be found in Claim 1 which recites the following after the listing of the R^1 Markush group members:

> wherein R^1 and R^2 of $-NR^1R^2$ may be connected by a linking group E to give a substituent of the formula



wherein E represents a bond, (C1-C4) alkylene, or (C1-C4) heteroalkylene and the ring formed by R^1, E, R^2 and the nitrogen atom contains no more than 8 atoms;

Without acquiescing to the position of the Examiner, the Applicants have amended intervening claim 2 to delete the recitals the Examiner may have construed to negate the antecedent basis of claim 1.

In view of the above, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Response to the Rejection of Claims 61 and 62 as allegedly anticipated by Ishii et al.

As the Examiner knows, according to MPEP §2131, to anticipate a claim, the reference must teach every element of the claim. Base claim 60 has been amended to set forth that the R^2 member is a heteroaryl group having one or two heteroatoms in the heteroaryl ring structure. The reference compound of Ishii et al. has four nitrogen atoms in its heteroaryl ring system.

In view of the above, the Applicants respectfully request that the above rejection be reconsidered and withdrawn.

Response to the Rejection of Claims 61 and 62 as allegedly anticipated by Nazareth et al.

The reference compound in Nazareth is a 4-pyrimidyl compound. The Applicants have amended their base claim to exclude subject matter wherein heteroaryl is 4-pyrimidyl. Support for this amendment is as noted above.

In view thereof, the Applicants respectfully request that the above rejection be reconsidered and withdrawn.

Response to the Rejection of Claims 1, 2, 36, 43, 44, 58, 59, 61, 62, 89, and 97 as allegedly anticipated by Iwata et al.

The referenced compound from Iwata et al. is not a compound according to Formula I of any of the base claims. R^2 is an optionally substituted heteroaryl group. The sulfonamide N atom of the referenced Iwata et al. compound is not covalently bound to an

heteroaryl group but rather has a heteroalkyl or alkyl linker therebetween. The subject claims do not recite that R^2 is heteroaryl-alkyl or heteroaryl-heteroalkyl.

Furthermore, turning now to the methods claims, base claim 43 recites "A method of treating a disease state characterized by abnormally high low density lipoprotein particles or cholesterol levels in the blood, which method comprises administering to a mammalian subject in need thereof..." Iwata et al. disclose methods of antagonizing platelet activating factors, and *not* a method of treating a disease state characterized by abnormally high low density lipoprotein particles or cholesterol levels in the blood.

In view of the above, the Applicants respectfully request that the above rejections be reconsidered and withdrawn.

Response to the Rejection of Claims 61 and 62 as allegedly anticipated by Posner et al.

Posner et al. are alleged to disclose a compound of Formula I. However, Formula I sets forth that R^2 is heteroaryl. The compounds of Posner et al. have no heteroaryl member attached directly or indirectly to the sulfonamide nitrogen atom. Rather, the N atom of the heteroaryl ring of the Posner et al. compound is N-atom of the sulfonamide group. In those embodiments of the instant invention wherein R^1 and R^2 are taken together with E to form a heterocyclic ring with the sulfonamide N atom, R^2 is itself heteroaryl. Thus, such embodiments are also distinguishable from the Posner et al. compound. The Posner et al. compound lacks any cyclic heteroatom other than the sulfonamide N atom.

In view of the above, the Applicants respectfully request that the above rejections be reconsidered and withdrawn.

Response to the Rejection of Claims 61 and 62 over U.S. Patent No. 4,881,969.

Without acquiescing to the position of the Examiner and in order to facilitate examination of the instant application, the Applicants have amended Claim 61 to recite "substituted or unsubstituted (C2-C10) alkyl" in place of "substituted or unsubstituted (C1-C10) alkyl." Applicants thank the Examiner for indicating that the subject matter in Claim 100 would be allowable and thus have sought to amend the compound base claim accordingly.

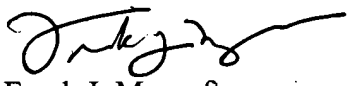
In view of the above, the Applicants respectfully request that the above rejections be reconsidered and withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



Frank J. Mycroft
Reg. No. 46,946

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 925-472-5000
Fax: 415-576-0300
Attachments
FJM:fjm
60372537 v1